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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/884,183	06/19/2001	Bret S. Weinstein	45421/RAS/W397	2814

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EXAMINER	
WOITACH, JOSEPH T	
ART UNIT	**PAPER NUMBER**
1632	

DATE MAILED: 07/14/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/884,183	WEINSTEIN, BRET S.	
	Examiner	Art Unit	
	Joseph T. Woitach	1632	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *17 February 2006*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *5 and 6* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *5, 6* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

This application filed June 19, 2001, claims benefit to provisional application 60/212,812, filed June 19, 2000.

Applicant's amendment filed February 17, 2006 has been received and entered. Claim 5 has been amended. Claims 1-4 and 7-20 have been canceled. Claims 5-6 are pending and currently under examination.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claim 7 rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention is withdrawn.

Cancellation of claim 7 has rendered the rejection moot.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 5-6 stand rejected under 35 U.S.C. 102(b) as being anticipated by Lee *et al.* (Nature 329:669-674, April 1998).

Claim 5 has been amended to indicate that the step of allowing the animals to breed is preceded by determining their teleomere length. The amendment to claim 5 is noted by Applicant, and it is argued that Lee *et al.* fail to provide a determination step prior to breeding as required by the amended claims. See Applicants amendment filed February 17, 2006, page 5. Applicant's arguments have been fully considered, but not found persuasive.

Examiner recognizes that for the breeding of G2-G6, Lee *et al.* do not teach that each successive generation is tested before mating, however wild type and G1 is tested and known (see page 671, first column). In this case, the teaching of Lee *et al.* who provides the analysis of Go/WT and G1 and the subsequent breeding and analysis for research purposes anticipate the instant claims. Lee *et al.* teach a mouse where the teleomere length has been determined, and provide analysis of the mice for experimental purposes. Lee *et al.* provide a first population of mice and consecutive breeding of said progeny to provide six generations of offspring, and analyze the teleomere length of each corresponding generation (see figure 1(1) for example). Further, Lee *et al.* analyze the correlation ion each generation of teleomere length and affects on the reproductivie system, in particular the germ cells of both the female and male germ cells (see figures 1(d) and 2 for example).

Again, it is noted that neither claims 5 nor 6 have any active step wherein the teleomere length is specifically modified, and given the guidance of the present specification requires simply the mating of two animals, and relying on the inherent property of the animal to result in any given type of progeny.

Claims 5-6 rejected under 35 U.S.C. 102(b) as being anticipated by Shiels *et al.* (Nature 399:316-317, May 27, 1999) is withdrawn.

Examiner agrees that the teaching of Shiels *et al.* fails to teach the claimed method as specifically amended. See also Applicants amendment filed February 17, 2006, page 6. Applicant's arguments have been fully considered, and found persuasive.

Conclusion

No claim is allowed.

As noted previously, at the time of filing and today there exists multiple lines of inbred animals (mice, dogs, cats, cattle,...) and while the skilled artisan would acknowledge that there are phenotypic differences among various lines, none of the phenotypes are correlated with teleomere length (for example the predisoposition of one line of mice to dabetes or susceptability to carcinogens). To the contrary rather than teleomere length, other genotypic factors are important in determining the phenotype of a given animal (see for example review of Festing (Neurobiology 20:23-244, 1999)). Moreover, it is further noted that this is consistent with Applicant's own views that it is not teleomere length by itself that may affect a phenotype, rather the mechanisms that control it (see Weinstein et al., Exp Gerontol. (2002 May) 37(5):615-27), and that the breeding of favorable phentotypes in laboratory animals may result in this loss of control not a consequence of teleomere length itself.

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

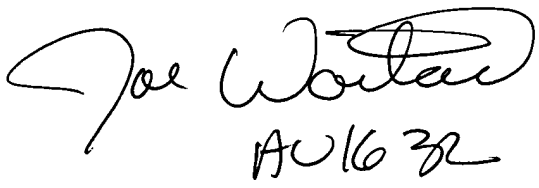
A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Joseph Woitach whose telephone number is (571) 272-0739.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ram Shukla, can be reached at (571) 272-0735.

Any inquiry of a general nature or relating to the status of this application should be directed to the Group analyst Dianiece Jacobs whose telephone number is (571) 272-0532.

Joseph T. Woitach



(for example, phlebotomy, chronic infection, skin wounding, petatectomy) might be able to elicit an age-dependent phenotype in old $mTR^{-/-}$ mice. Preliminary analysis indicates that some G_1 $mTR^{-/-}$ animals in two independent colonies exhibit erosive dermatitis, which might indicate a defect in dermal stem cells (H.W.L. and R.A.D., and E. H. Herrera, J. M. C. Caballero and M.A.B., unpublished observations). At present the limited sample size does not allow us to assign this phenotype unambiguously to the mTR deficiency, although studies are continuing.

On the basis of previous studies in lower organisms that show a temporal lag between telomere loss and diminished cell viability, we suspected that substantial telomere loss would be required before a compromised clinical condition became apparent. Thus, as described[20], we have produced additional generations (G_2, G_3, G_4, G_5 and G_6) of $mTR^{-/-}$ mice from successive matings of homozygous-null intercrosses. Avoidance of inbreeding in the later generations was achieved through regular cousin-mating schemes[29] of offspring produced from 20 different G_1 $mTR^{-/-}$ matings; these G_1 mating pairs were in turn derived from 10 different $mTR^{+/-}$ intercrosses.

Reproductive system

Reproductive function is highly dependent on proper germ-cell expansion and development. All matings proved to be productive up to the fifth generation. However, a statistically significant decline in litter size became apparent in the G_4 intercrosses (Fig. 1a; G_4 $P = 0.021$ compared with G_1). No offspring were produced from eight different G_6 intercrosses. Both sexes appear to be affected, as only one in eight G_6 males and one in eight G_6 females produced a litter when mated to a wild-type partner.

Male reproductive system. As the number of spermatocyte

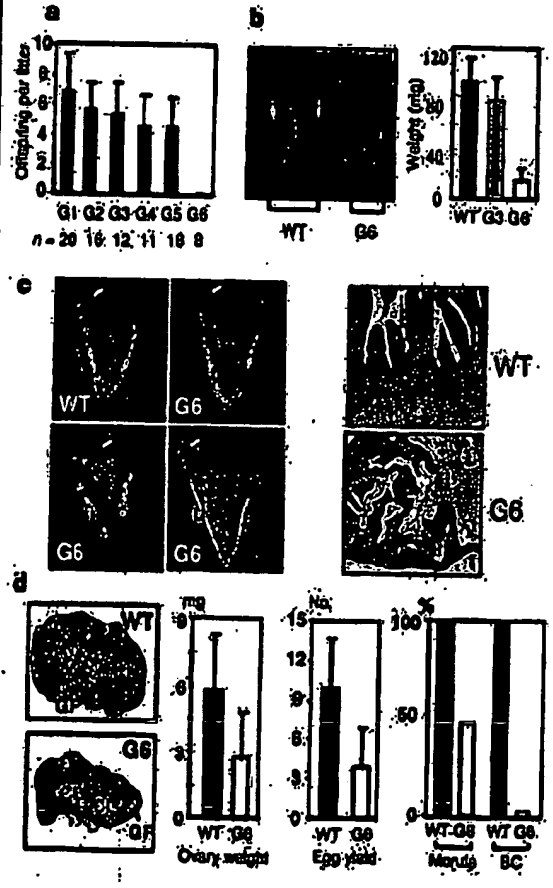


Figure 1 Effects of lack of telomerase on the mouse reproductive system. a, Impaired reproductive function in late-generation mTR-deficient mice. Males aged 6–12 weeks and females aged 4–12 weeks of the same generation of telomerase-deficient mice were mated over a period of 2 months or longer; *n* indicates the number of mating pairs examined. The *P* values of each generation were calculated compared with G_1 (G_2, $P = 0.063$; G_3, $P = 0.070$; G_4, $P = 0.021$; and G_5, $P = 0.004$). b, Testicular atrophy and testes weights. Scale bar, 5 mm. c, Uterine horns. Grossly dissected uterine horns (u) and ovaries (arrows) (scale bar, 5 mm) and haematoxylin and eosin (H&E) staining (magnification ×50). d, Ovarian structure and function. Oestrus-matched ovaries are shown at ×50 magnification (left). E, endometrium; M, myometrium; GF, Graafian follicle; CL, corpora lutea. The graphs show a weight comparison of ovaries, average egg yields following natural mating with a wild-type stud male, and the percentage of *in vitro* development of pre-implantation embryos. BC, blastocyst.

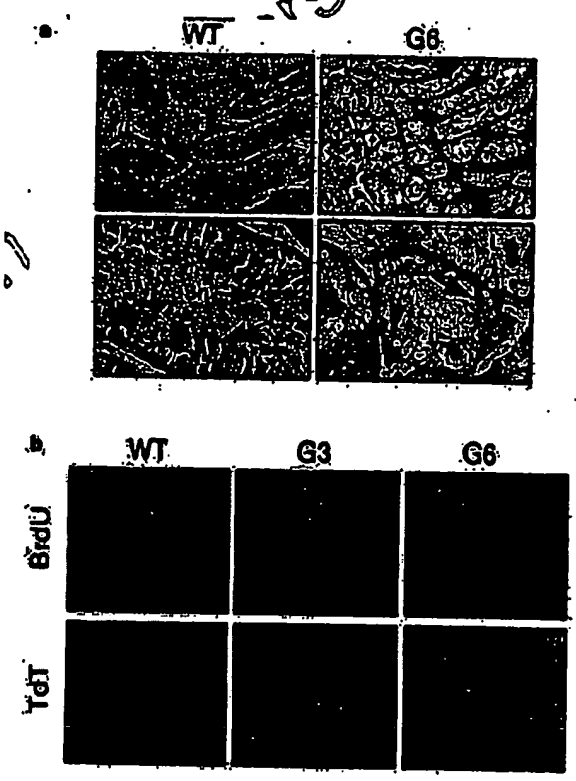


Figure 2 Proliferation and apoptosis in the male germ-cell compartment. a, Histology of WT and G_6 testis. Top: sections at low magnification (×50) through WT testes and representative G_6 testes show the diminished cellularity in the G_6 testes although there are some tubules undergoing nearly normal spermatogenesis (left edge of G_6 section). At higher magnification (×200 (bottom)), all stages of spermatogenesis are well represented in WT seminiferous tubules, whereas most G_6 tubules lack spermatogenesis yet retain Sertoli cells. In the G_6 testes, the apparent local accumulation of Leydig cells in the interstitium is secondary to contraction of the seminiferous tubules and an overall decrease in testis volume. Sr, Sertoli cell; L, Leydig cell; Sg, spermatogonia; Sc, primary spermatocyte; ES, early spermatid; LS, late spermatid. b, Comparative BrdU incorporation and TUNEL assays. Relative to WT samples, there was an approximate reduction in BrdU-positive nuclei (arrows) of three- to fivefold for G_3 mice and greater than 20- to 100-fold for G_6 mice. In the TUNEL (TdT) assay, G_3 seminiferous tubules and G_6 tubules with adequate cellularity for comparative analysis possessed many TUNEL-stained germ-cell nuclei (arrows), whereas only an occasional apoptotic cell was detected in the WT samples. Magnification ×100.